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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/501,173 | 07/09/2004 | Henryk Struszczyk | 7008USO1 | 6041 |

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| EXAMINER | |
|---|---|
| WHITE, EVERETT NMN | |
| ART UNIT | PAPER NUMBER |
| 1623 | |

| MAIL DATE | DELIVERY MODE |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/501,173 | STRUSZCZYK ET AL. | |
| | Examiner | Art Unit | |
| | Everett White | 1623 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *01 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/01/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 1, 2007 has been entered.

2. The amendment filed June 1, 2007 has been received, entered and carefully considered. The amendment affects the instant application accordingly:

(A) Claims 1, 4, 10, 21 and 33 have been amended;
(B) Comments regarding Office Action have been provided drawn to:
  (I) 103(a) rejections over Claims 1-9, which have been maintained for the reasons or record.
  (II) 103(a) rejection over Claims 10-42, rendered moot by new ground of rejection over newly cited US Patent.

3. Claims 1-42 are pending in the case.

4. The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior Office action.

### *Claim Rejections - 35 USC § 103*

5. Claims 1-9 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Goosen et al (US Patent No. 4,942,129) in view of Struszczyk et al (US Patent No. 5,554,445) for the reasons disclosed on pages 2-4 of the Office Action filed September 20, 2006.

6. Applicant's arguments filed June 1, 2007 have been carefully considered but they are not persuasive. Applicants argue against the rejection on the ground that the references do not disclose a gel agent consisting essentially of a chitosan salt" because the Gossen et al patent teaches alginate gels that may include chitosan and the Struszczyk et al patent teaches microcrystalline chitosan. This argument is not

persuasive since the phrase "consisting essentially" which is now recited in the instant claims is an open-ended phrase, which allows for the presence of additional components in the chitosan-calcium complex.

Accordingly, the rejection of Claims 1-9 under 35 U.S.C. 103(a) as being unpatentable over the Goosen et al patent in view of the Struszczyk et al patent is maintained for the reasons of record.

***New Ground of Rejection***

7. Claims 10-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nies et al (EP 650999 A1, already of record) or Hashimoto et al (U.S. Patent No. 5,474,989, already of record) in view of Goosen et al (US Patent No. 4,942,129, already of record) or Struszczyk et al (US Patent No. 5,554,445. already of record).

Applicants claim a method of preparing chitosan salt gels, comprising the steps of: (a) degrading chitosan in an aqueous acidic solution with enzymes, said solution having a chitosan concentration of ≥ 0.5 wt% for a desired time and at a desired temperature; (b) deactivating said enzymes after said desired time is completed; (c) adding an aqueous basic solution to said enzyme/aqueous chitosan mixture to attain $4.0 \leq pH \leq 6.0$; and (d) continuously mixing said mixture until a gel of a chitosan salt forms, wherein said gel contains ≥ 0.5 wt% chitosan having an average molecular weight ≥ 10 kD, a polydispersity ≥ 2.0, deacetylation degree ≥ 65% and wherein said complex has a water retention value ≥ 300%, pH ≤ 6.9 and a calcium (II) ions bound to the chitosan gel at a content ≥ 0.1 wt% relative to chitosan. Applicants also claim a method of preparing a gel of a chitosan salt, comprising the steps of: (a) degrading chitosan hydrolytically, said chitosan being dissolved in an aqueous acidic solution, said solution having a chitosan concentration of ≥ 0.5 wt% for a desired time and at a desired temperature; (b) adding an aqueous basic solution to the mixture of step (a) to attain $4.0 \leq pH \leq 6.0$; and (c) continuously mixing the product of step (b) until a gel of a chitosan salt forms. Applicants further claim a method of preparing a chitosan salt gel, comprising the steps of: (a) degrading chitosan with an oxidizing agent, said chitosan being dissolved in an aqueous acidic solution, said solution having a chitosan

concentration of ≥ 0.5 wt% for a desired time and at a desired temperature; (b) adding an aqueous basic solution to the mixture of step (a) to attain 4.0 ≤ pH ≤ 6.0; and (c) continuously mixing the product of step (b) until a gel of a chitosan salt forms.

The Nies et al publication discloses production of gels of chitosan effected by dissolving the chitosan and an acid chelate complex in water, wherein gels are obtained by adding to the solution polyvalent metal/acid salts in which the chitosan is only slightly soluble (see Derwent Abstract). The abstract discloses the salts used in the production of the chitosan gels may be selected as calcium -carbonate, -sulphate, -phosphate or -oxalate.

The instantly claimed methods differ from the method of the Nies et al publication by claiming a step that involves degrading chitosan with enzymes, degrading chitosan hydrolytically, and degrading chitosan with an oxidizing agent.

The Hashimoto et al patent shows that the degradation of chitosan is well known in the art. The Hashimoto et al patent teaches methods of obtaining low molecular weight chitosan which include enzyme treatment of chitosan, and subjecting chitosan to treatment with compounds such as hydrogen peroxide (an oxidizing agent), nitrite ion, an alkali or an acid (see column 2, lines 63-67). The step of degrading chitosan in the instant claims is within the scope of reducing the molecular weight of chitosan. See column 3, line 17, wherein chitinase or chitosanase may be selected as the enzymes to cause degradation of the chitosan's molecular weight.

The instantly claimed methods also differ from the Nies et al publication by claiming that the said gel contains ≥ 0.5 wt% chitosan having an average molecular weight ≥ 10 kD, a polydispersity ≥ 2.0, deacetylation degree ≥ 65% and wherein said complex has a water retention value ≥ 300%, pH ≤ 6.9 and a calcium ion content ≥ 0.1 wt% relative to chitosan.

However, the Goosen et al and Struszcyk et al patents show that the presence of these properties in chitosan material are known in the art. The Goosen et al patent discloses penetration of chitosan into a calcium alginate gel matrix to form chitosan-alginate microcapsules using chitosan derivatives having a molecular weight (MW) greater the 10 kD and pH of 6.5 (see column 11, 2nd paragraph), which fall within the

MW and pH ranges disclosed in the instant claims. The Struszczyk et al patent shows that the polydispersity, deacetyation degree and water retention values disclosed for chitosan in the instant claims are also known in the art. See Example 1 of the Struszczyk et al patent wherein microcrystalline chitosan is characterized as having an average molecular weight of 78000, deacetylation degree of 72%, and water retention value of 1240%, which embraces the values disclosed in the instant claims.

One of ordinary skill in this art would be motivated to combine the teachings of the Nies et al publication with the teachings of the Hashimoto et al, Goosen et al and Struszcyk et al patents since each of the documents teach or suggest the preparation of drug compositions comprising chitosan.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to include in the method of preparing a chitosan salt gel of the Nies et al publication a process step that degrades or lower the molecular weight of the chitosan in view of the recognition in the art, as evidenced by the Hashimoto et al patent, that the dissolution rate of pooly water-soluble drugs were improved by mixing the poorly water-soluble drugs with a low molecular weight chitosan. It also would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the chitosan product used in the method of preparing a chitosan salt gel of the Nies et al publication with chitosan material having specific molecular weight, polydispersity, deacetylation degree, water retention, pH and chitosan gel content properties in view of the recognition in the art, as evidenced by the Goosen et al and Struszczyk et al patents, that the chitosan material having such properties increases the effectiveness of chemicals by reducing the dosage of dressing chemicals as well as their losses into the environment.

8. Applicant's arguments with respect to Claims 10-42 have been considered but are moot in view of the new ground(s) of rejection.

***Summary***

9. All the claims are rejected.

***Examiner's Telephone Number, Fax Number, and Other Information***

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Everett White whose telephone number is 571-272-0660. The examiner can normally be reached on 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-066127. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

E. White

E. White

6/15/07

Shaojia A. Jiang
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